REMARKS/ARGUMENTS

Claims 1, 6, 8-12, 19-25, 30, 32-35 and 40 are active in this application. Support for Claims 1 and 12 is found in Claim 7, Claim18, and page 7, lines 8-9. No new matter is added by these amendments.

As amended herein, the present claims are to a modified enzyme in which glycine at amino acid 38 in a *L. brevis* or *L. kefir* rec-R-alcohol dehydrogenase enzyme is replaced with aspartic acid and which has increased NAD(H) affinity compared to the wildtype enzyme. This modified enzyme is not described in Hummel et al.

Hummel et al. describes reducing the basic nature of the coenzyme-docking site by exchanging positively charged for uncharged amino acids and/or by replacing neutral or positively charged amino acids with negatively charged amino acids (see column 1, lines 54-61). As described in the specification on page 3, lines 14-19, referring to the work described in Hummel et al. (with reference to the PCT equivalent WO 99/47684):

> Other mutants in which an additional replacement of a neutral amino acid by an acidic amino acid (G38D) was performed along with the above-mentioned replacements of basic amino acids by neutral amino acids (replacements R39L, K48M as well as the charge neutral replacement A9G), indeed exhibited broadening of the coenzyme affinity towards NAD(H), but was also considerably unstable and obtainable only with low yields.

This statement is supported by the data presented in the Table on page 22 of the present application. In particular, Applicants direct the Examiner's attention to column 3: "Mutant 2" rows 5 and 6 where the thermal stability was measured (also refer to page 21, lines 3-4 noting that Mutant 2 is per WO99/47684, i.e., Hummel et al.).

The data presented in this table also demonstrates that the claimed G38D modified enzyme had significantly higher thermal stability at both 30°C and 42°C relative to the Hummel et al mutant. In addition, the claimed G38D modified enzyme had improved NAD

affinity relative to wildtype (referring to the data and supporting discussion in the paragraph bridging pages 22 and 23).

In sum, Hummel et al. does not describe synthesizing a G38D modified enzyme that is not coupled to other mutants such as those described in Example 5 (col. 17) of Hummel et al. Furthermore, there description that by preparing such a mutant that it would be more thermally stable than what is described in Hummel et al. As a result, the present claims are not anticipated by nor would have been obvious in view of the Hummel et al. disclosure.

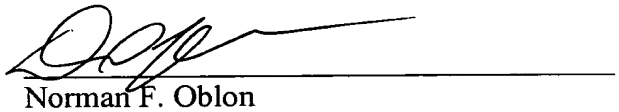
Withdrawal of this ground of rejection is requested.

The rejection of Claim 7 under 35 U.S.C. § 112, second paragraph is obviated by the cancellation of this claim.

Applicants submit that the present application is now ready for allowance. Early notification of such allowance is requested.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.



Norman F. Oblon
Attorney of Record
Registration No. 24,618

Daniel J. Pereira, Ph.D.
Registration No. 45,518

22850

Tel: (703) 413-3000
Fax: (703) 413 -2220